# THE APPLICATION OF THE CALCULUS TO THE MEDICAL SCIENCES.

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In the following I am giving a few ideas on the above subject in connection with a Calculus recently published, entitled *Einführung in die Höhere Mathematik für Naturforscher und Aerzte*, by Dr. J. Saltpeter.[1] It is a book of unusual merit. The representation is rigorous and lucid. The book contains many examples illustrating the application of Calculus in developing mechanical and chemical laws and processes. Although the author has intended the book for the use of students in the natural sciences and medicine, it is equally well adapted for engineering students.

The applications of the Calculus to the different branches of the medical and allied sciences is of comparatively recent origin. The originators are still with us. The science of mathematics is new. It is only about 200 years since the Calculus was invented (Leibnitz, 1646–1716 and Newton, 1642–1727). The first account of it was published by Newton in 1693. But the real advance of the mathematical sciences has taken place during this and the last generation. The application of Calculus to any of the sciences including the technical sciences, dates back only to the middle of the last century. Most of the schools of engineering in this country and abroad have been founded within the last fifty years or so. The scientific development of all the natural sciences does not date very far back, and the makers of the sciences have died within our generation or are still living.

I recall the address delivered by the founder of scientific pathology, Rudolph Virchow, before the students of the University of Berlin on the occasion of his seventieth birthday (1891), at which he entertained his hearers with an account of the most incredible theories and absurd views that prevailed in natural science when he first began the study of the subject.

In this connection it is interesting to read the presidential address of Dr. S. Weir Mitchell to the Congress of American Physicians and Surgeons held in 1891,[2] from which I quote the following (p. 163):

"When I was yet a lad there were then alive men who could recall the day when what a patient said, and the physician saw and felt, were all that a case of disease had to tell him. The limitations they suffered under, lured or drove them into attempts to classify, and minutely to multiply the signs of disease, until what they believed they saw and felt represented impossible refinements in symptomatology."

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[1] Gustav Fischer, Jena, 1913.

[2] Transactions of the Congress, Vol. II, New Haven, 1892.

It should be distinctly understood that the operations of the so-called elementary mathematics are not sufficient for the study and the interpretation of natural phenomena and processes. This can be accomplished only by Calculus. In fact, Calculus seems to be the very language of nature. All processes in nature proceed by infinitely small degrees. Consider the growth of a tree or of any organic matter. During the interval of time required to give a glance at the tree, the tree has either grown or decayed. While this growth or decay is so small that it cannot be measured by the most delicate instruments, yet it is as definite a quantity as any finite quantity is. The growth of a tree during a month or a year is made up of the infinitely large number of the infinitely small growths during the infinitely small periods of time. Again, a vessel of water is heated. The infinitely small increase in the temperature of the water is not the same for the different infinitely small periods of time. We say the amount of growth during the different infinitely small periods of time varies. Now these infinitely small numbers which represent the infinitely small increases can be compared with each other just as finite numbers can be compared. The infinitely small increase in the temperature of the water during one infinitely small period of time might be any number of times as large as the infinitely small increase during the same or a different infinitely small period of time.

Also, just as the infinitely small quantities can be compared with each other, so can infinitely large quantities be compared. One infinitely large quantity might be a number of times larger or smaller than another infinitely large quantity. If a piece of material be divided into a number of parts and each part divided again, and if we imagine this division continued until each particle is so small that it cannot be detected by the most powerful microscope, then no matter how far the division is carried on, the particles, although infinitely small, have a definite extension and weight. The sum of the infinitely large number of the infinitely small particles make up the original piece of material. The infinitely large number representing the number of infinitely small particles at one stage of the division might be many times larger or even infinitely times as large as the infinitely large number representing the number of infinitely small particles at another stage of the division. For the term infinitely small the term infinitesmal is used.

The operations of Calculus enable us to study a process during a given period of time by means of the changes which are taking place during the infinitely small intervals of time.

Calculus is divided into two branches, the Differential and the

Integral Calculus. In the first, problems relating to infinitesimal changes are studied and in the second, problems leading to the sum of an infinite number of infinitesimals are considered. Thus: If a body is being heated at a certain rate of increase of temperature, its rate of expansion at any instant may be obtained by means of Differential Calculus. Or again, if a particle moves under the action of certain forces its velocity at any instant can be determined by Differential Calculus and the distance travelled by Integral Calculus.

Helmholtz, the inventor of the ophthalmoscope, who is as well known to the mathematician and physicist as he is to the physician, was led to the results in mathematics from the observation of nature. Professor Leo Königsberger of Heidelberg[3] says of Helmholtz: "He obtained his mathematical problems—this is certainly the only true way, but also one to be pursued by so great a master—directly from observation of nature. . . . On this account there is to be found in all his works a great many results, which are interesting even from a purely mathematical point of view, but which uncover deep and intelligible natural laws." By purely mathematical investigation based upon known natural laws, new laws have been derived which have predicted phenomena, which in turn have been verified by observation and experiment. To show what mathematics is capable of accomplishing and what might be expected of this powerful instrument if applied to the study of the human body, I cite the following instances:

One of the most remarkable discoveries in Physics—the law of conical refraction—was made as the direct result of mathematical investigation.

By means of Calculus Sir William Rowen Hamilton found that a point, when looked at through a crystalline plate cut in a certain direction, ought to appear not as a point but as a ring. Lloyd, of Dublin, verified Hamilton's results experimentally.[4]

As a direct result of mathematical analysis, Professor Michael I. Pupin, of Columbia University, has invented a process which has considerably increased the distance of communication by telephone.[5]

The discovery of wireless telegraphy owes its inception to mathematics.

The old idea was that electricity could be transmitted from one place to another only by means of metallic conductors, such as wires, etc. The air was considered an insulator or non-conductor of electricity. James Clerk Maxwell, by purely mathematical deductions, arrived at the conclusion that electricity, like light, is propagated by ether vibrations; that light, radiation and electric radiation are essentially the same and that electro-magnetic waves obey all the laws of optics. A full development of the subject is given in his work, "A Treatise on Electricity and Magnetism," first published in 1873.[6]

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[3] Herman von Helmholtz's Untersuchungen über die Grundlagen der Mathematik and Mechanik, 1896, p. 2.

[4] Humphrey Lloyd, Elementary Treatise on the Wave Theory of Light, Third Edition, p. 209, London, 1873.

[5] The Electric Review, Vol. XL, No. 2, 1902, p. 53.

As Maxwell's results were opposed to the accepted views, and as his theories were only the result of mathematical deductions the most eminent men of science doubted their validity. Maxwell[7] himself said: "There appears to be in the minds of these eminent men some prejudice or *a priori* objection, against the hypothesis of a medium, in which the phenomena of radiation of light and heat and the electric actions at a distance, take place." Even Heinrich Hertz[8] (1857–1894), who ultimately became the champion of Maxwell's mathematical theories of electricity, said: "Notwithstanding the greatest admiration I hold for Maxwell's mathematical conceptions, I have not always felt quite certain of having grasped the physical significance of his statements."

In 1879, the Berlin Academy of Sciences offered a prize for a problem which practically meant the experimental verification of Maxwell's electro-magnetic theory. Hertz took up the problem and succeeded in verifying experimentally Maxwell's mathematical theories. It was, therefore, through mathematics that the so-called Hertzian waves were discovered which Marconi has made use of so ingeniously in connection with one of the most wonderful practical inventions that has ever astonished mankind.

Dr. F. H. Garrison,[9] in an admirable contribution, says: "Most of the working theorems of modern physical chemistry were stated *a priori* as mathematical consequences of the second law of Thermodynamics by Gibbs, many years before they were actually tried out, and in some cases, rediscovered in the laboratory."

Fresnel[10] (Fresnel's wave surface), in a letter to Young, said: "Without doubt I have often wanted the spur of vanity to excite me to pursue my researches in moments of disgust and discouragement. But all the complements which I have received from Arago, Laplace, etc., never gave me so much pleasure as the discovery of a theoretical truth or the confirmation of a calculation by experiment."

Mathematicians planted the first seeds of accurate and scientific medicine, but unfortunately for the science it was at a time when the sciences of physics and chemistry were only about to spring into being, when the law of gravitation was not as yet established, when Calculus was not yet invented.

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[6] Clarendon Press, Oxford.

[7] Ibid., Vol. II, third edition, p. 492, 1892.

[8] Electric Waves, London, 1893, p. 20.

[9] Physiology and the Second Law of Thermodynamics, New York Medical Journal, Vol. XC p. 494.

[10] Peacock. Life of Young.

René Descartes (born in France in 1596, died in Stockholm in 1650), the inventor of the analytic geometry, was an accomplished physicist. He wrote a treatise on physiology entitled L'Homme (1662), which is said to be the first physiology published. Sir M. Foster,[11] speaking of the book, says: "But his main idea, that the problems of man ought to be treated in the same way as the problems of the rest of nature, made itself felt and produced effects in after times."

Giovanni Alphonso Borelli (born at Naples in 1608, died 1679), was one of the leading mathematicians and physicists of his day. Under him the University of Pisa became the most famous school for mathematics and medicine. The new methods of physical mathematical research led him to the study of the mechanism of the human body, which he has incorporated in a treatise on animal motion *De motu animalium.* In the preface of the book he states that his purpose in science is "to ornament it and enrich it by mathematical demonstrations."

Both Descartes and Borelli were inspired in their work by the teachings and writings of Galileo (born at Pisa in 1564, died 1642). When Professor of Mathematics at the University of Pisa, Galileo invented the thermometer or thermoscope. It is said that when Galileo was but eighteen years of age and a student in medicine, when sitting in the Cathedral of Pisa his attention was drawn to a huge swinging lamp, which still hangs there. He noticed, that whether the arc through which the lamp swung was large or small, the oscillations occupied the same interval of time. That observation led him to the invention of the pulsilogon, which, though imperfect, was hailed with wonder and delight by the physicians of the day, and was soon taken into general use."[12]

Molecular force has placed each particle of which the bones, the nerves, and the muscles are made up, in its proper place. Speaking of the molecules which make up the human body, John Tyndall[13] says: "Unless the existence of law be denied and the element of caprice be introduced, we must conclude that, given the relation of any molecule of the body to its environment, its position in the body might be determined mathematically." Mathematics might perhaps help us to discover the laws which govern the changes that take place in the cells and tissues of the human organism, and enable us to direct and redirect these changes. To understand the vital organism of the blood and to determine the blood pressure and the velocity of the blood current in the arteries and veins, a knowledge of the physical-mathematical laws of hydro-dynamics is necessary. The mechanism of labor in normal births is a physical process based on mechanical mathematical principles.

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[11] Lectures on the History of Physiology, Cambridge, 1901, p. 62.

[12] Viviani. Vita di Galileo.

[13] Scientific Limit of the Imagination, London, 1870, p. 61.

Ophthalmology, the science of the structure, functions, and diseases of the eye, may be justly considered a branch of applied mathematics. A. Gullstrand of the Medical Faculty of the University of Upsala won, in 1912, the Nobel Prize for his work on the internal mechanism of accommodation to which he applies the operations of Calculus. It is of interest to note that in the Medical Department of the University of Berlin, Professor Gutzmann is giving, during this Winter-Semester, a course in *Mathematische Analyse normaler und pathalogischer Sprachklänge.*

The human skeleton, including the various articulations, is constructed in strict accordance with mathematical laws. When the end of a long bone, say the femur, is examined, it is found to be made up of interlacing osseous plates, technically called "concelli." Professor J. Engel,[14] of Prague, says: "Not without a purpose does the structure seem to differ in the various arches, the use here of vertical columns, there of oblique abutments, is certainly intended for something else than to merely delight the eye of the anatomist by pretty carvings." Professor Herman von Meyer, of Zurich, in 1867, presented before the Naturforscher Gesellschaft some specimens which were to demonstrate the inner structure of the human thigh bone. Culman, the founder of graphical statics, who happened to be present, recognized at once in the course and in the arrangement of the concelli, the trajectories of graphical statics, and he was greatly surprised at the similarity between the mysterious workings of nature and the mode of construction followed by scientific engineers. The subject of the construction of bones was next taken up by Professor Wolff, of Berlin, a man combining a thorough training as a physician with a rare knowledge and understanding of mathematics, and who was advised and aided in his work by Culman himself. He has embodied the result of his twenty years' investigation in a work, entitled, "The Law of the Transformation of Bones,"[15] which is interesting alike to the physician, the engineer, and the mathematician. He found that the shape and inner structure of a bone depended upon the direction and the amount of the stress acting upon it, and that changes in the stress will cause definite changes in the form and the structure of the bone, in accordance with strict mathematical laws. And just as a pathological stress will cause abnormal changes in a bone, so, on the other hand, a deformed bone may be made to return to its normal state by well-directed changes in the stress acting upon it. These principles Wolff has made the basis of a new method of the treatment of various deformities of bones, notably club-foot, without resorting to operative measures.

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[14] Sitzungsberichte der Wiener Akademie der Wissenschaften, 1851.

[15] Julius Wolff, Das Gesetz der Transformation der Knochen, Berlin, 1892.

It would appear that the present generation of physicians are not in a position to follow ideas in the medical sciences if they are represented by means of mechanical-mathematical principles. On that account, investigators of the medical sciences along mechanical-mathematical lines are often obliged to give the results of their investigations without the method by which they have arrived at their conclusion.

The discoveries of Zuppinger in the treatment of fractures of bones is based on mechanical-mathematical considerations. Dr. Th. Christen has embodied Zuppinger's discoveries in a book,[16] from the preface of which I quote the following:

"Right here an objection which we meet at every turn, that Zuppinger's ideas may be very interesting, perhaps even theoretically correct, but that they are too 'mathematical,' too 'abstract,' and not intelligible to the medical fraternity, must be answered. . . . We have, however, owing to the sentiment at present prevailing among our colleagues of the medical profession, made it our duty to keep the principal part of the text of this book free from every mathematical formula. . . . In fact a large number of therapeutical errors which are still taught and practised are based on wrong mechanical conceptions. . . . To give only an approximate idea of the importance of every improvement in this field of science it may be stated that (according to Hoffa) about two-thirds of the premiums paid in workmen's compensation insurance in Germany are the result of poorly healed fractures of bones."

In the preface to his masterly work,[17] written "in erster Linie für Mediziner und Zoologen," Otto Fischer states that he has endeavored to derive and represent the kinematic principles in an elementary way, so that the book may be more generally understood, but in Chapters IV and VI he was obliged to take recourse to the Differential and Integral Calculus, because without it he could not obtain the principles sufficiently general and intact.

Dr. Friedrich von Müller, Professor of Medicine in the University of Münich, on November 17, 1909, addressed the Medical Society of Münich on the topic, "Welche Mittelschulvorbildung ist für das Studium der Medizin wünschenswerth?" The address and the discussion appears in the Münchener medizinischen Wochenschrift, 1910, No. 19. To make it accessible to a larger circle of readers it has been published in 1911 in phamphlet form by B. G. Teubner in Leipzig. I quote from it the following:

"If, therefore, physics is to be taught in our universities in such a way as the physicians shall need it later in life, an absolutely different fundamental view must be taken, and this is possible only when a higher degree of mathematical knowledge is assumed. Today, not only for the study of physics, but also for the study of chemistry and physiology, a thorough mathematical knowledge is necessary. Physical chemistry which has found numerous applications in medicine and which has become indispensible in our laboratories, assumes a knowledge of higher mathematics. The text-book on physical chemistry by Nernst is for this reason unintelligible to me and, indeed, to most of my pupils. For the same reason I can follow only in part even the text-book for physicians on osmotic pressure and the theory of iones written by Hamburger. There are many students of medicine to whom the important works of Otto Frank on the problems of the circulation of the blood are only in part intelligible, because they presuppose a knowledge of higher mathematics."

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[16] Allgemeine Lehre von den Knochenbrüchen, Leipzig, 1913.

[17] Die Kinematik organischer Gelenke, Braunschweig, 1907.

During the last few years a great advance has taken place in the $x$-ray treatment of gynecological diseases and deep cancers, so-called deep treatment. This was made possible by inventing exact instruments for measuring the penetration and the dosage of administered rays. These instruments owe their inception to Calculus.[18]

Christen's results in the $x$-ray treatment relating to high penetration by hard tubes, which he has obtained by means of higher mathematics, have been verified by the practical and experimental work of the radiologists and gynecologists.

The invention and the improvement of some of the instruments used in diagnosis like the manometer, sphygmograph, etc., has been helped by the Calculus and even by its most advanced branches (Differential Equations).

It is an unfortunate peculiarity of the science of mathematics that, while a fair knowledge of one of its special branches might enable the student to follow intelligently the solutions of the simpler problems in this branch, yet even an intimate knowledge of that branch might not enable him to understand in the least degree the results in another branch. The ideas represented by the one branch and the symbolism in which these ideas are expressed are wholly different from the ideas and symbolism of another branch. On that account a specific example illustrating the application of mathematics to any branch of science can only be followed by those who have a knowledge of this branch of mathematics. Those readers who are familiar with the processes of Calculus are referred to the books and articles on the Medical Sciences named below, in which Calculus is applied. These together with the books and articles mentioned in this paper are those to which I had access and the list, therefore, is quite necessarily limited.[19]

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[18] Th. Christen, Messung und Dosierung der Röntgenstrahlen, Ergänzungsband 28 of the Fortschritte auf dem Gebiete der Röntgenstrahlen, Hamburg, 1913.

There are investigators in the medical sciences whose work involve principles of mechanics, which in turn are based on mathematical analysis. To this class of investigators belong I. Traube, of Charlottenburg, M. Ascoli, of Pavia, A. E. Taylor, of Philadelphia, H. Zuppinger, of Basel, L. Bürker, of Tübingen, L. Asher, of Bern, S. Garten, of Leipzig, H. Sellheim, of Freiburg, E. Münzer, of Prag, R. Tigerstedt, of Helsingfors, Ch. Bouchard, of Paris, R. Höber, of Kiel.

How Professor Traube has been helped by the results of physical mathematical investigations in his work on the relation of surface-tension to osmosis, digestion, narcosis, hemolysis, serodiagnosis, etc., may be judged from the following statement made by him:[20] "I attribute the clarification of my views to the fact that my attention was called to an important theorem of which I had not previously been aware, the thermodynamic demonstration of which is originally due to the great mathematical physicist Willard Gibbs."

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[19] Th. Christen, Neue Wege in der Pulsdiagnostik, Zeitschrift für klinische Medizin, Vol. 71, 1910, pp. 390 to 401.

O. Frank, Endliche Ausbauchungen einer aufgespannten elastischen Membran, Zeitschr. für Biol., Vol. 50, 1908, p. 281.

S. A. Arrhenius, Immunochemistry, 1907.

K. Hürthle, Experimentalkritk der Frank'schen Theorie der elastischen Manometer, Pflüger's Archiv, Vol. 137, 1910-11, p. 153.

C. Schaefer, ibid., pp. 250 to 258.

J. Wolff, Ueber die normale und pathalogische Architectur der Knochen., Arch. Path., Anat., Physiol., 1901.

W. B. Hardy, Physiological articles in the Proceedings of the Royal Society, Vols. 86–88, 1911–1913.

O. Fischer, Physiologische Mechanik, in Encyklopaedie der Mathematischen Wissenschaften, Vol. IV, I, II, Heft I, 62 to 126, Leipzig, 1904. The index on the literature of the subject contains a list of 21 text-books and treatises and 421 monographs.

O. Frank, Prinzipien der graphischen Registrierung, Zeitschrift für Biologie, Vol. 53, 1910, pp. 429 to 456.

Th. Christen, Ueber die Anwedung zweier physikalischer Gesetze auf den Blutkreislauf, Zeitschrift für experimentelle Pathologie und Therapie, Vol. VII, 1910, p. 783.

O. Frank, Kritik der elastichen Manometer, Zeitschrift für Biologie, Vol. 54, 1903, p. 445.

K. Hürthle, Betrachtungen über die theoretischen und praktischen Bestrebungen, Instrumente zur Registrierung der im Kreislauf auftretenden Druckschwankungen herzustellen. Pflüger's Archiv für die gesammte Physiologie, Vol. 137, 1911, pp. 145 to 152.

O. Frank, Dynamik der Membranmanometer und der Lufttransmission, Zeitschrift für Biologie, Vol. 50, 1908, p. 309.

I. Petter, Die Leistungen des Sphygmographen. Zeitschrift für Biologie, Vol. 51, 1908, p. 335.

O. Frank, Prinzipien der Konstruktion von Schreibhebeln, Zeitschrift für Biologie, Vol. 45, 1904, p. 480.

H. von Recklinghausen: Was wir durch die Pulsdruckkurve and durch Pulsdruckamplitude über den grossen Kreislauf erfahren, Archiv für experimentelle Pathologie und Pharmakologie, Vol. 56, p. 1.

Th. Christen, Die Pulsdiagnostik auf mathematisch-physikalischer Grundlage, Zeitschrift für experimentelle Pathologie und Therapie, Vol. VI, 1909, pp. 125 to 170.

H. J. Hamburger, Osmotischer Druck und Ionenlehre in den medizinischen Wissenschaften, 3 Vols., 1902–04.

[20] Pflüger's Archiv, Vol. 132, 1910, p. 511.

The great progress of the technical sciences during the last few decades is to a large extent due to the support it has received from mathematics. No one is taking up the study of the technical sciences without a more or less extended mathematical equipment. But to the study and investigation of the medical sciences, so far only a few have brought a deeper mathematical knowledge, and it is, therefore, the more surprising to learn how these few representatives have in a comparatively short time done so much toward advancing the medical sciences along mathematical lines. It augors well for the adaptability of the medical sciences to mathematical interpretation and investigation and encourages the hope that, with the increase in the number of investigators with mathematical training and ability, a more intimate knowledge of the organic laws governing the human body will be obtained and a corresponding increase in the efficiency of the methods for curing its ailments will result. While there is no medical school in this country or in Europe, which, as far as I could find, requires of its medical students a knowledge of the Calculus, there are many universities in Europe in which a course in Calculus is offered for natural science and medical students. In the Department of Chemistry in the University of Pennsylvania a few years ago a course in Calculus was made obligatory with all students.

The rapid increase during the last few decades in things material which has brought about abrupt changes in all aspects of life, is pressing also for sweeping changes in the fundamental principles of education. There is a tendency to reduce both in school and college, the amount of required mathematics. It is a fortunate circumstance, however, that we have among us men of high educational ideals with a knowledge of the past and a clear understanding of the requirements of the future, who are stemming the tide and saving as much as possible of our educational heritage, until an adjustment of the new conditions will bring those who are carried with the current to the realization and to a sober view of what comprises true education, true progress, and true happiness. The Provost of the University of Pennsylvania, with a deep knowledge of the history of the sciences and of his own specialty, an ardent investigator, with broad sympathies for the needs of those who are to be leaders, is in favor of a curriculum for a liberal education to include a thorough course in mathematics and in the ancient languages. While mathematics still possesses the educational powers as it did at that time of Gauss who found the main charm of the science in its *utter inutility*, it has during the last few decades turned into a subject of *indispensable utility*, not only in the study of the technical sciences, but also in the study of the natural and allied sciences.